UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,746	05/23/2007	Andreas Bergmann	2582.012	9538

23405 7590 03/12/2010

HESLIN ROTHENBERG FARLEY & MESITI PC
5 COLUMBIA CIRCLE
ALBANY, NY 12203

EXAMINER	
COUNTS, GARY W	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
03/12/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,746	BERGMANN ET AL.	
	Examiner	Art Unit	
	GARY W. COUNTS	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *20-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. EP 04003295.5.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/02/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-19 in the reply filed on December 23, 2009 is acknowledged.

It is noted that in the response filed 12/23/09 Applicant stated that they elect claims 1-19 and new claim 23. Examiner called Kathy Smith Dias, Attorney on 02/26/10 to explain that there was no new claim 23 listed and that claim 23 was previously presented as a kit claim. Kathy Smith Dias stated that there was no new claim 23 and that the election was for claims 1-19 only.

Currently, claims 1-23 are pending. Claims 20-23 are withdrawn as being directed to non-elected inventions. Claims 1-19 are under examination.

Information Disclosure Statement

2. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Specification

3. The disclosure is objected to because of the following informalities: the specification on page 7, lines 5-8 discloses that claim 1 relates to the teaching of the present invention. Advantageous and currently preferred embodiments of the invention are described in the subclaims. The reference to claims in the specification is improper because the claim numbering is subject to change throughout prosecution and thus can cause discrepancies between the specification and the claims. It is recommended to remove any reference to claims from the specification. Appropriate correction is required.

4. The disclosure is objected to because of the following informalities: The specification on page 11 discloses descriptions of figures 3a and 3b. However, a review of the drawings submitted 05/23/07 indicates figures 1-4 and does not provide for figures 3a and 3b. Also, the specification does not provide a description for figure 4 filed 05/23/07. Appropriate correction is required.

5. The disclosure is objected to because of the following informalities: The specification does not provide headings for the different sections contained within the disclosure. For example, pages 10-11 discloses descriptions of the figures but does not provide a heading for the brief description of the drawings.

Appropriate correction is required.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) THE NAMES OF THE PARTIES TO A JOINT RESEARCH AGREEMENT.
(e) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC.
(f) BACKGROUND OF THE INVENTION.
    (1) Field of the Invention.
    (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(g) BRIEF SUMMARY OF THE INVENTION.
(h) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(i) DETAILED DESCRIPTION OF THE INVENTION.
(j) CLAIM OR CLAIMS (commencing on a separate sheet).
(k) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(l) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

6. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while appearing to be enabling for a method for detecting C-terminal fragments of preproendothelin-1 (SEQ ID NO:1) in sample selected from the group consisting of whole blood, plasma or serum, wherein the sample is collected from a human patients suffering from cardiovascular disease, systemic inflammatory response syndrome, and sepsis by contacting the sample with antibodies which specifically bind within amino acids 168-181, 184-203 and 200-212 of preproendothelin-1, does not reasonably provide enablement for any and all antibodies and any and all sequence positions within amino acids 93-212 of preproendothelin-1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. The factors that must be considered in determining undue experimentation are set forth in *In re W*ands USPTQ2d 14000. Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.

The instant claims are directed to an in vitro method for the determination of the formation of endothelins in serious diseases, in particular cardiovascular disease, inflammations, sepsis and cancer, in whole blood, plasma or serum of a human patient for purposes of medical diagnostics, wherein the formation of endothelin-1 (SEQ ID NO: 2) and big endothelin-1 (SEQ ID NO:3) is determined by determining those C-terminal fragments of preproendothelin-1 (SEQ ID NO:1) which are recognized by antibodies which bind to peptides which correspond to peptide sequences in the range of amino acids 93-212 of preproendothelin-1.

The specification fails to teach any and all antibodies bind to any and all sequence combinations of amino acids 93-212 of preproendothelin-1. The specification on page 12, lines 1-8 discloses the peptide fragment determined is a c-terminal fragment to which two antibodies bind which bind to peptides having amino acid sequences which correspond to the positions 168-181 and 200-212 of preproendothelin-1. The specification on pages 22-23 discloses assays wherein antibodies were raised against the positions 136-148, 168-181, 184-203, and 200-212 and utilized in assays with samples from cardiological and sepsis patients. However, the specification clearly teaches that in the assay wherein antibodies directed against amino acids 136-148 were used that it was not possible to obtain measured values raised compared with healthy persons. Thus, it appears that the only working examples which provide for the detection of C-terminal fragments of preproendothelin-1 are directed to antibodies which bind within amino acids 168-181, 184-203, and 200-212 of preproendothelin-1. Further, antibodies which bind to c-terminal fragments of preproendothelin-1 are not well known

in the art and as shown by Applicant not all sequences contained within amino acids 93-212 provide for the detection of the C-terminal fragments in samples from patients suffering cardiological or sepsis conditions. The specification fails to provide for the use of any and all antibodies to bind to any and all positions of sequences within amino acids 93-212 and provide for the detection of C-terminal fragments of preproendothelin-1 in samples from patients suffering cardiovascular, inflammations, sepsis and cancer. At best the detection C-terminal fragments of preproendothelin-1 (SEQ ID NO:1) can be detected by contacting the sample from the patients with antibodies that specifically bind within amino acids 168-181, 184-203 and 200-212 of preproendothelin-1. Thus such is not seen as sufficient to support the breath of the claims one skilled in the art cannot practice the claimed invention without undue experimentation, because in order to have a high level of predictability, one skilled in the art would have to know that all antibodies to amino acids 93-212 of preproendothelin-1 would bind to any position within amino acids 93-212 and that these antibodies would detect the C-terminal fragments of preproendothelin-1 in samples from patients suffering from cardiovascular diseases, inflammations, sepsis, and cancer.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 the recitation “serious diseases” is vague and indefinite because it is unclear what applicant is trying to encompass. The term "serious" is a relative term which renders the claim indefinite. The term "serious" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 1 is vague and indefinite because of the recitation “serious diseases, in particular cardiovascular diseases, inflammations, sepsis and cancer”. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation serious diseases, and the claim also recites in particular cardiovascular diseases,

inflammations, sepsis, and cancer which is the narrower statement of the range/limitation.

Claim 1, the phrase "in particular" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 1 the recitation “those C-terminal fragments of preproendothelin-1” is vague and indefinite because it is unclear what is included in those. It is unclear if the C-terminal fragments are all SEQ ID NO. 1 or other sequences other than SEQ ID NO. 1. It is unclear what the term encompasses and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. See also deficiency found in claim 4.

Claim 1 is vague and indefinite because it is unclear how the formation of endothelin-1 and big endothelin-1 is determined in the whole blood, plasma or serum because the claim is directed to determining preproendothelin-1 and there are no actual method steps to correlate or determine endothelin-1 or big endothelin-1 with that of the preproendothelin-1. Therefore, how can one positively determine if endothelin-1 or big endothelin-1 has been formed or not in the sample. Further, there do not appear to be actual method steps for detecting the C-terminal fragments of preproendothelin-1. The claim is indefinite in reciting “determining” those C-terminal fragments of preproendothelin-1 which are recognized by antibodies which bind to peptides which correspond to peptide sequences in the range of amino acids 93-212 of preproendothelin-1” because the term “determining” appears to intend a mental step; hence, it is unclear if applicant actually intends positive active method steps in the

claim. It is suggested but not required to delete the term “determining” and replace it with –detecting--. Method claims should clearly set forth the various method steps in a positive, sequential manner using active tense verbs such as mixing, reacting and detecting. Method claims should also clearly state each component used in the method and the relationship of the various components, and should not be a mere cataloging of parts. The claims should also conclude with a step relating the method result to the purpose of the method, preferably to the purpose as also set forth in the preamble of the claim.

Claim 2 the recitation “wherein the determination in biological fluid” is vague and indefinite because it is unclear if Applicant is referring to the whole blood, plasma or serum recited in claim 1 or if Applicant is referring to another biological fluid.

Claim 2 the recitation "the peptide fragment" there is insufficient antecedent basis for this limitation.

Claim 5 the recitation “a C-terminal fragment”” is vague and indefinite because it is unclear if Applicant is referring to the C-terminal fragment recited in claim 1 or if Applicant intends another C-terminal fragment.

Claim 6 the recitation “the peptide fragments” there is insufficient antecedent basis for this limitation. Further, it is unclear what peptide fragments Applicant is referring to.

Claim 7 the recitation "another accelerated test" is vague and indefinite because it is unclear what Applicant is trying to encompass. The phrase "another accelerated test" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be

reasonably apprised of the scope of the invention. Further, the term “accelerated” is a relative term which renders the claim indefinite. The term "accelerated" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 9 the recitation “the antibodies which are obtained" there is insufficient antecedent basis for this limitation.

Claim 9 is indefinite in reciting improper Markush language in reciting “synthetic peptide which is selected from the peptides” because it appears to intend to limit the scope of the synthetic peptides in the claims but improperly defines it as such. Perhaps, Applicant intends, “synthetic peptide which is selected from the group consisting of (SEQ ID NO: 4), (SEQ ID NO: 5) and (SEQ ID NO: 6).

Claim 11, line 3 the recitation "the liquid reaction mixture" there is insufficient antecedent basis for this limitation.

Claim 11, line 7 the recitation “the peptide fragment” there is insufficient antecedent basis for this limitation.

Claim 12 , the phrase "in particular" renders the claim indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 12 the recitation “the cyanine type” there is insufficient antecedent basis for this limitation.

Claims 13 -19 provide for the use of the method of claim 1, but, since the claims do not set forth any steps involved in the method/process of diagnosing, determining severity or prognosis, and monitoring or provide steps of cardiac or cancer diagnosis, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 13-19 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Conclusion

11. No claims are allowed.

12. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kido et al., (Eur. J. Biochem. 244, 1997, pages 520-526) disclose the sequence analysis of preprendothelin-1 (p. 520-521).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GARY W. COUNTS whose telephone number is (571)272-0817. The examiner can normally be reached on M-F 8:00 - 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571) 272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/ Gary W. Counts/
Examiner, Art Unit 1641

/Melanie Yu/
Primary Examiner, Art Unit 1641
3/11/10